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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,440	03/17/2004	Martha Karen Newell	V0139.70060US01	4035
7590	11/06/2006			EXAMINER
Helen C. Lockhart, Ph.D. Wolf, Greenfield & Sacks, P.C. 600 Atlantic Avenue Boston, MA 02210				VANDERVEGT, FRANCOIS P
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/802,440	NEWELL, MARTHA KAREN
	Examiner F. Pierre VanderVegt	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 16 August 2006.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-11 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) 7-11 is/are allowed.  
 6) Claim(s) 1-6 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

This application is a continuation of U.S. Application Serial Number 09/711,022; which is a continuation of U.S. Application Serial Number 09/277,575, which claims the benefit of the filing date of provisional applications 60/082,250; 60/094,519 and 60/101,580.

Claims 1-11 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment filed August 16, 2006, no outstanding ground of rejection is maintained.

The following represents a new ground of rejection.

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanciulli et al (Oncology Res. [1996] 8(3):111-120; V on form PTO-892, of record) in view of Ianiello et al (Cancer [1996] 78(1):63-69; W on form PTO-892, newly cited).

Fanciulli teaches the treatment of ADRIAMYCIN-sensitive [claim 6] and ADRIAMYCIN-resistant [claim 5] MCF-7 human breast cancer cells with simultaneous local contact with a combination of the metabolic modifying agent glucose and the chemotherapeutic agent lonidamine (LND) (Abstract in particular), as acknowledged by Applicant on page 14 of the response filed August 16, 2006. Fanciulli is silent regarding whether glucose increases the mitochondrial membrane potential of the tumor cell, however silence about a particular property does not necessarily constitute its absence. It is noted that the claim does not recite the degree to which the metabolic modifying agent raises mitochondrial membrane potential, so even the tiniest amount of an increase would satisfy the metes and bounds of the claim. The assertion in the claim that mitochondrial membrane potential is increased appears to merely constitute a further characterization of an otherwise old property of the metabolic modifying agent. Accordingly, absent a showing to the contrary or a recitation in the claim of a degree of increased mitochondrial

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mitochondrial membrane potential not realized by the prior art, the amount of glucose administered to the tumor cells by Fanciulli is reasonably assumed to increase mitochondrial membrane potential to at least a minimal degree and therefore satisfies the metes and bounds of the limitations of the claim.

Fanciulli does not teach the chemotherapeutic agent Cisplatin.

Ianiello teaches that LND selectively inhibits the energy metabolism of neoplastic cells and increases the permeability of cell membranes. Ianiello further teaches that clinical trials have suggested that LND may act synergistically with alkylating agents, cisplatin, and anthracyclines (Abstract in particular). It is noted that ADRIAMYCIN is an anthracycline compound [claim 2]. Ianiello further teaches that LND does not have any overlapping toxicity with other cytotoxic agents (page 64, last paragraph of column one in particular). Ianiello teaches the treatment of breast cancer patients with a combination of LND and cisplatin. Ianiello teaches that LND was able to reverse the acquired resistance of breast or ovarian cancer cell lines to anthracyclines and cisplatin and that LND enhanced the activity of cisplatin, epirubicin, and vindesine against cell clones with intrinsic resistance to cytotoxic treatments (page 67, column one in particular).

It would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Fanciulli and Ianiello and administer cisplatin or an anthracycline in combination with LND and glucose to tumor cells. One would have been motivated to combine the teachings with a reasonable expectation of success by the teachings of Fanciulli on the effects of LND on metabolism in tumor cells and the teachings of Ianiello that LND potentiates the effectiveness of other cytotoxic agents against tumor cells that have an intrinsic or acquired resistance to cytotoxic agents.

### *Conclusion*

3. Claims 7-11 are allowed.
4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

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shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.  
Patent Examiner  
October 26, 2006

*David A. Saunders*  
DAVID A. SAUNDERS  
PRIMARY EXAMINER